IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	MDL Docket No. 2738
This Document Relates To All Cases	

DEFENDANTS JOHNSON & JOHNSON AND LLT MANAGEMENT, LLC'S OPPOSITION TO THE PLAINTIFFS' STEERING COMMITTEE'S RESPONSE TO THE COURT'S APRIL 30, 2024 MEMORANDUM AND ORDER REGARDING JUDGE WOLFSON'S *DAUBERT* OPINION ON GENERAL CAUSATION

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This Court held in its April 30, 2024 Order that because there is evidence that the "medical science has changed over the last three years," "it may be appropriate, upon a proper showing by Defendants, to reconsider" Judge Wolfson's prior general causation *Daubert* rulings.[1] The Court further acknowledged "that Defendants should be allowed to contest previous *Daubert* holdings by [Judge Wolfson] should Defendants be able to identify any incorrect application of Rule 702."[2] Plaintiffs nonetheless seek to prevent Defendants Johnson & Johnson and LLT Management, LLC from seeking the exclusion of plaintiffs' general causation experts (Drs. Carson, Clarke-Pearson, Cote, Harlow, Kane, McTiernan, Moorman, Siemiatcyki, Singh, Smith, Smith-Bindman and Wolf). Specifically, plaintiffs' brief seeks to demonstrate that "there is no basis for a Rule 702 challenge" because recent legal and scientific developments support plaintiffs' experts' general causation opinions. Plaintiffs' legal argument misapprehends Judge Wolfson's prior ruling and entirely ignores the import of recent amendments to Rule 702.

Plaintiffs also rely heavily on select scientific literature—O'Brien 2020, Woolen 2022 (which was co-authored by plaintiffs' expert Dr. Smith-Bindman)

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1 (Memorandum Order ("April 30 Order") at 4, Apr. 30, 2024 (ECF No. 32122).)

2 (*Id*. at 5.)

and O'Brien 2024—and the pronouncements by select regulatory bodies to support their argument that there is a consistent association between talcum powder use and ovarian cancer. But ***none*** of these scientific studies or regulatory bodies has reached the conclusion that perineal talc use can cause ovarian cancer; and, in fact, contain further evidence that discredits the opinions of plaintiffs' experts' methodology and opinions.

For these reasons, plaintiffs' attempt to prevent this Court from hearing and considering the reliability of their experts in light of the changed legal and factual landscape since Judge Wolfson's prior *Daubert* ruling should be denied. Defendants can—and have, in their Motion to Exclude Plaintiffs' Experts' General Caution Opinions—demonstrated (in compliance with this Court's mandate) that: (1) Judge Wolfson's general causation *Daubert* opinion misapplied Rule 702, in light of the 2023 amendments clarifying Rule 702; and (2) recent scientific developments further undermine plaintiffs' experts' causal theories and highlight the unreliability of those opinions.

BACKGROUND

Judge Wolfson ruled in 2020 that because three of plaintiffs' experts (Drs. Anne McTiernan, Daniel Clarke-Pearson and Arch Carson) all purported to apply the Bradford Hill framework for assessing general causation, their opinions—which defied the scientific consensus—were admissible and their approach to

scientific principles was a matter of "weight" that should be decided by jurors based on cross-examination. *See In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Pracs. & Prods. Litig.*, 509 F. Supp. 3d 116, 148, 163, 166-67, 172, 175 (D.N.J. 2020) (invoking the word "weight" no fewer than 55 times).

Since that ruling, there have been a number of scientific developments that undermine plaintiffs' experts' causal theories and highlight the unreliability of their methodologies. Most notably, O'Brien 2020—the largest pooled study of the cohort data ever performed on the issue—found "no statistically significant association between . . . use of [talcum] powder in the genital area and risk of ovarian cancer."[3] The study also found "no clear dose-response trends for duration and frequency of powder use in the genital area in relation to ovarian cancer risk."[4] Following the O'Brien 2020 pooled analysis, an article published in the journal *Gynecologic Oncology*, written by the lead authors of the O'Brien paper, concluded that "[g]iven the inability to attribute a clear causal factor to the observed associations, the lack of a good experimental model, the lack of a specific biomarker for powder-related carcinogenesis, and the inability to rule out

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[3] O'Brien, *Association of Powder Use in the Genital Area With Risk of Ovarian Cancer*, 323(1) JAMA 49, 56 (2020) ("O'Brien 2020") (Pls.' Br. Ex. 7). Although O'Brien 2020 was published before the MDL Court issued its ruling, it was not part of the experts' prior opinions and was not addressed in the *Daubert* ruling.

[4] *Id.*

confounding by indication, ***it is difficult to conclude that the observed associations are causal***. Furthermore, given the widespread use of powders and the rarity of ovarian cancer, the case for public health relevance is limited."[5]

Recent studies also highlight that the findings of plaintiffs' touted data are skewed by bias or confounding. For example:

- O'Brien 2023 confirmed that recall bias is "potentially driving some of the previously observed differences in effect estimates between studies collecting genital powder exposure status retrospectively versus prospectively."[6]

- The Goodman 2024 quantitative bias assessment similarly "demonstrates that recall bias alone may have a large impact on risk estimates" in case-control studies and "that recall bias results in a bias away from the null" (i.e., away from a finding of no association).[7]

- Davis 2021—a study co-authored by plaintiffs' expert, Dr. Moorman—acknowledged that "[w]hen the time period was limited to women who were interviewed prior to 2014 (i.e., before ongoing lawsuits about genital powder use which had extensive media coverage), the results were attenuated and no[t] . . . significant," which "highlight[s] the potential for recall bias in case-control

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[5] Wentzensen & O'Brien, *Talc, Body Powder, and Ovarian Cancer: A Summary of the Epidemiologic Evidence* 163 Gynecol. Oncol. 199, 207 (2021) ("Wentzensen & O'Brien 2021") (Ex. 1 to Declaration of Jessica Davidson ("Davidson Decl.")) (emphasis added).

[6] O'Brien, *Douching and Genital Talc Use: Patterns of Use and Reliability of Self-Reported Exposure*, 34(3) Epidemiology 376, 378, 383 (2023) ("O'Brien 2023") (Ex. 2 to Davidson Decl.).

[7] Goodman, *Quantitative Recall Bias Analysis of the Talc and Ovarian Cancer Association*, 7 Glob. Epidemiol. 1, 3 (2024) ("Goodman 2024") (Ex. 3 to Davidson Decl.).

studies."[8]

- Chang 2024 demonstrates that any reported association may actually be with douching, a confounding factor that most studies did not account for.[9]

Plaintiffs' claim that some of the newly published literature supports their conclusions; it does not. For one thing, much of it was published by paid plaintiffs' experts in this litigation, and many of those papers have been criticized. For example, the National Cancer Institute ("NCI") has discredited Woolen 2022 (a study co-authored by Dr. Smith-Bindman), stating that "because of the structure of [Woolen 2022's] analysis, ***the results should be interpreted with care***."[10] And O'Brien 2024—which relied, in part, on retrospective questionnaires and imputed data—does not support plaintiffs' theories of general causation either because much of the paper is based on data that where made up. As such, this study is, at bottom, guesswork; presumably for that reason, the authors cautioned that the

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[8] Davis, *Genital Powder Use and Risk of Epithelial Ovarian Cancer in the Ovarian Cancer in Women of African Ancestry Consortium*, 30(9) Cancer Epidemiol. Biomarkers Prev. 1660, 1664-65 (2021) ("Davis 2021") (Ex. 4 to Davidson Decl.).

[9] *See* Chang, *Use of Personal Care Product Mixtures and Incident Hormone-Sensitive Cancers in the Sister Study: A U.S.-Wide Prospective Cohort*, 183 Environ. Int'l 1, 5 (2024) ("Chang 2024") (Ex. 5 to Davidson Decl.).

[10] Ovarian, Fallopian Tube, and Primary Peritoneal Cancer Prevention (PDQ®)–Health Professional Version, National Cancer Institute ("NCI 2024 PDQ"), https://www.cancer.gov/types/ovarian/hp/ovarian-prevention-pdq (last updated Mar. 6, 2024) (emphasis added).

"results do not establish causality and do not implicate any specific cancer-inducing agent."[11]

Consistent with the recent scientific evidence, numerous U.S. regulatory and medical bodies have reiterated their rejection of plaintiffs' proffered causal theory. For example:

- The Centers for Disease Control and Prevention's ("CDC") website was updated in October 2023 and does not list talc use as a risk factor for ovarian cancer.[12]

- The American College of Obstetricians and Gynecologists ("ACOG") similarly updated its frequently asked questions on ovarian cancer in May 2022 and does not list talc as a risk factor for ovarian cancer.[13] This is consistent with the organization's prior statement that "[t]here is no medical consensus that talcum powder causes ovarian cancer."[14] It also aligns with ACOG's Committee Opinion #619, recommending talc application as a modality to reduce postoperative wound complications in obese patients.[15]

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[11] O'Brien, *Intimate Care Products and Incidence of Hormone-Related Cancers: A Quantitative Bias Analysis*, J. Clin. Oncol. (2024): JCO-23, at 13 ("O'Brien 2024") (Pls.' Br. Ex. 8) (emphasis added); *see also id.* at 14 ("[O]ur findings . . . do not pinpoint a specific cause or mechanism . . . .").

[12] Ovarian Cancer Risk Factors, Centers for Disease Control and Prevention, https://www.cdc.gov/ovarian-cancer/risk-factors/index.html (last updated Oct. 26, 2023).

[13] Ovarian Cancer FAQs, American College of Obstetricians and Gynecologists, https://www.acog.org/womens-health/faqs/ovarian-cancer (last updated May 2022).

[14] Talc Use and Ovarian Cancer, American College of Obstetricians and Gynecologists (Sept. 11, 2017), https://www.acog.org/news/news-releases/2017/09/talc-use-and-ovarian-cancer.

[15] Committee Opinion No. 619: Gynecologic Surgery in the Obese Woman, American College of Obstetricians and Gynecologists (Jan. 2015, reaffirmed

(cont'd)

- The Society of Gynecologic Oncology identifies established risk factors for ovarian cancer on its website and does not list talc.[16]

- In 2023, the CDC funded ACOG to form an expert review panel that included members from a number of national societies, including, among others, the American Cancer Society, American Society of Clinical Oncology, the National Comprehensive Cancer Network ("NCCN"), and others.[17] This group reviewed the literature and identified "research gaps" in every area of ovarian cancer research, including risk factors. Talc was not mentioned in any of the research gaps. Their review found "heterogeneity in the studies on the use of talcum powder and ovarian cancer risk."[18]

- The NCCN found that "[e]nvironmental factors have been investigated, such as talc, but so far they have not been conclusively associated with the development of this neoplasm."[19]

- The National Cancer Institute PDQ, which was updated in March 2024, states that "the data are inadequate to support an association between perineal talc exposure and an increased risk of ovarian cancer."[20]

2019), https://www.acog.org/-/media/project/acog/acogorg/clinical/files/committee-opinion/articles/2015/01/gynecologic-surgery-in-the-obese-woman.pdf.

16 Ovarian Cancer Risk Factors, Society of Gynecologic Oncology, https://www.sgo.org/patients-caregivers-survivors/caregivers/ovarian-cancer-risk-factors/ (last visited Aug. 17, 2024).

17 Burke, *Executive Summary of the Ovarian Cancer Evidence Review Conference*, 142(1) Obstet. Gynecol. 179, 191 (2023) (Ex. 6 to Davidson Decl.).

18 *Id.* at 183.

19 Clinical Practice Guidelines in Oncology: Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer, National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1453 ("NCCN Guidelines").

20 NCI 2024 PDQ.

- The American Cancer Society concluded this year that "[t]he weight of the evidence does not support an association between ovarian cancer and genital exposure to talc-based powder."[21]

- All of these recent public statements mirror the views of the FDA, which "did not find that the data submitted presented conclusive evidence of a causal association between talc use in the perineal area and ovarian cancer."[22]

While IARC recently reclassified talc as "probably carcinogenic to humans," it made clear that "a causal role for talc could ***not*** be fully established" in light of "biases in how talc use was reported in the epidemiological studies."[23] As a member of the IARC working group explained, because "[s]elf-reporting can sometimes be unreliable . . . the human study evidence was ***not*** strong enough to say that talc causes ovarian cancer."[24]

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[21] Cancer Facts & Figures 2024, at 23, American Cancer Society, https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf ("Cancer Facts & Figures 2024").

[22] Letter from Steven M. Musser, Ph.D., Deputy Dir. for Sci. Operations, Ctr. for Food Safety & Applied Nutrition, to Samuel S. Epstein, M.D., Cancer Prev. Coalition, Univ. of Ill. – Chi. School of Pub. Health, at 1 (Apr. 1, 2014) ("FDA Denial Letter") (Ex. 7 to Davidson Decl.).

[23] Press Release No. 352, IARC, *IARC Monographs Evaluate the Carcinogenicity of Talc and Acrylonitrile*, IARC Monographs Volume 136 (July 5, 2024) ("IARC Press Release"), https://www.iarc.who.int/wp-content/uploads/2024/07/pr352_E.pdf (emphasis added).

[24] Statement of Katie O'Brien, Science Media Centre Spain, https://sciencemediacentre.es/en/talc-classified-probably-carcinogenic-humans-iarc (last visited July 13, 2024) ("O'Brien Statement") (emphasis added); *see also* Stayner, *Carcinogenicity of Talc and Acrylonitrile*, Lancet Oncol. (2024), at 2 ("Stayner

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In light of the scientific advancements and the 2023 amendments to Rule 702 that clarified Rule 702 and "outline[d] a consistent and concerning misapplication of Rule 702," this Court held that the parties may file new *Daubert* motions where the motions identified "either: (1) that [Judge] Wolfson's previous [o]pinion demonstrably fail[ed] to adhere to Rule 702 as clarified by the 2023 amendments; or (2) new science is shown to directly contradict or challenge [Judge] Wolfson's previous findings."[25] In accordance with this Court's guidance, defendants submitted a *Daubert* motion seeking to exclude plaintiffs' experts' general causation opinions. (*See* Defs.' Mot. to Exclude General Causation Ops. (Doc. 33008).)

ARGUMENT

I. JUDGE WOLFSON'S *DAUBERT* RULING MISAPPLIED RULE 702.

Plaintiffs argue that that because Judge Wolfson issued an "exhaustive opinion" that purported to evaluate both sides' expert evidence and invoked the "preponderance of evidence" standard, that ruling correctly applied Rule 702. (Pls.' Br. at 4.) Plaintiffs also posit that the Final Screening Assessment performed by Health Canada "applied the same general causation methodology" as Judge

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2024") (Pls.' Br. Ex. 2) (IARC's reclassification is based on "'***limited***' evidence that talc causes ovarian cancer in humans") (emphasis added).

[25] (April 30 Order at 5-6.)

Wolfson, and thus, its findings somehow illustrate that the Court's prior ruling was correct. (*Id.* at 5-9.) Plaintiffs' arguments should be rejected because they misapprehend the Court's prior ruling, ignore the import of recent amendments to Rule 702 and confuse the standard that Health Canda applied in its assessment.

First, plaintiffs insist that the Rule 702 ruling "***appl[ied] the preponderance of evidence standard***." (Pls.' Br. at 5.) But the phrase "preponderance of the evidence" appears only three times in Judge Wolfson's prior *Daubert* ruling, each time as part of a case parenthetical. And plaintiffs' proffered opinions on biological plausibility (i.e., that talc causes ovarian cancer by inflammation) were deemed admissible because "Defendants ha[d] not introduced any evidence that this theory has been disproven as a matter of science," *In re Johnson & Johnson*, 509 F. Supp. 3d at 175, reflecting a "***revers[al]*** [of] the burden of proof" that is precisely the opposite of what Rule 702 demands. *See In re Onglyza (Saxagliptin) & Kombiglyze (Saxagliptin & Metformin) Prods. Liab. Litig.*, 93 F.4th 339, 345 (6th Cir. 2024) (emphasis added) (excluding opinion that the literature "should be interpreted as cause-and-effect unless there is compelling evidence to prove otherwise") (citation omitted).

Second, plaintiffs ignore the other key aspects of the recent amendments—namely, that the "court" (rather than a jury) must decide that all four of the substantive criteria for admissibility are satisfied, including that the "expert's

opinion reflects a reliable application of the principles and methods to the facts of the case." Fed. R. Evid. 702(d). As multiple courts construing these changes have explained, "Rule 702's recent amendments were drafted to correct some court decisions incorrectly holding 'that the critical questions of the sufficiency of an expert's basis, and the application of the expert's methodology, are questions of weight and not admissibility.'" *In re Onglyza*, 93 F.4th at 348 n.7 (quoting Fed. R. Evid. 702 advisory committee's note to 2023 amendment); *accord In re Paraquat Prods. Liab. Litig.*, MDL No. 3004, 2024 WL 1659687, at *4 n.9 (S.D. Ill. Apr. 17, 2024) ("The Advisory Committee thus appears to have found that courts had erroneously admitted unreliable expert testimony based on the assumption that the jury would properly judge reliability by assigning appropriate weight to an expert's opinion."), *appeal filed*.[26]

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[26] *See also Sardis v. Overhead Door Corp.*, 10 F.4th 268, 279, 284 (4th Cir. 2021) (treating fundamental reliability challenges as "generally questions of weight and not admissibility" is erroneous and constitutes an "abdicat[ion] [of a court's] critical gatekeeping role to the jury") (quoting Advisory Comm. on Evidence Rules, Agenda for Committee Meeting 105, 107 (Apr. 30, 2021)); *James v. Thompson/Ctr. Arms, Inc.*, No. 22-01781, 2024 U.S. Dist. LEXIS 55675, at *6 (N.D. Ohio Mar. 28, 2024) ("This is not merely a question of weight, to be decided by a jury. The expert's proponent bears the burden of demonstrating to me, by a preponderance of the evidence, 'the sufficiency of an expert's basis[] and the application of the expert's methodology.'") (quoting Fed. R. Evid. 702 advisory committee's note to 2023 amendment); *In re Acetaminophen - ASD-ADHD Prods. Liab. Litig.*, MDL No. 3043, 2023 U.S. Dist. LEXIS 224899, at *49-50 & n.27 (S.D.N.Y. Dec. 18, 2023) ("*In re Acetaminophen I*") ("[O]ne purpose of the amendment was to emphasize that '[j]udicial gatekeeping is essential . . . .'") *(cont'd)*

Defendants respectfully submit that Judge Wolfson's prior *Daubert* ruling was one of those incorrect holdings. For example, the decision states that "it is not for the Court to decide" whether plaintiffs' experts properly applied the Bradford Hill considerations such as strength of association, because doing so "would unnecessarily broaden the scope of this Court's role as a gatekeeper." *In re Johnson & Johnson*, 509 F. Supp. 3d at 164; *see also id.* at 171-72 (defendants' criticisms of plaintiffs' experts' approach to consistency factor of Bradford Hill reflected "a battle of the experts" and "relate[s] to the weight of their testimony"); *id.* at 175 ("jury will determine what weight to ascribe to th[e] scientific hypothesis" that talc causes ovarian cancer by inflammation). Courts applying the recently amended Rule 702 have recognized that this is not a proper approach because simply espousing a methodology (i.e., Bradford Hill) does not suffice to withstand a Rule 702/*Daubert* challenge. Rather, "district courts must ensure that '[t]he specific way an expert conducts such an analysis [is] reliable.'" *In re Acetaminophen I*, 2023 U.S. Dist. LEXIS 224899, at *56 (citation omitted) (excluding experts who engaged in similarly unreliable Bradford Hill causation analyses). Accordingly, the caselaw addressing amended Rule 702 makes clear

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(citation omitted); *West v. Home Depot U.S.A., Inc.*, No. 21-1145, 2024 WL 2845988, at *2 (N.D. Ill. June 5, 2024) (explaining "Rule 702 required amending because 'many courts have held that the critical questions of the sufficiency of an expert's basis, and the application of the expert's methodology, are questions of weight and not admissibility,' which is 'incorrect'") (citation omitted).

that the kinds of reliability challenges raised by defendants with respect to plaintiffs' general causation experts are admissibility questions for the Court rather than issues of weight to be sorted out by jurors after cross-examination.

Third, contrary to plaintiffs' claim, Health Canada's assessment does ***not*** "provide[] external validation of Judge Wolfson's ***legal*** approach to the reliability of the exact same evidence." (Pls.' Br. at 9 (emphasis added).) For starters, far from reaching a definitive conclusion on causation, Health Canada merely states that "the available data are indicative of a causal effect."[27] Indeed, Health Canada expressly noted that "there is some inconsistency between results from case-control studies versus cohort studies, in particular with respect to the degree of statistical significance."[28] It is precisely such inconsistency that has led the FDA to reject causality.[29] Health Canada also concluded that among "studies that provided some evidence of increased risk of ovarian cancer with increasing

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[27] Health Canada, *Final Screening Assessment: Talc ($Mg_3H_2(SiO_3)_4$) (Chem. Abstracts Serv. Registry No. 14807-96-6)* (Apr. 2021), at 36, https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/screening-assessment-talc.html ("Health Canada Screening Assessment"); *id.* at 45 ("While there may not be consensus within the scientific community regarding the interpretation of the epidemiological information, after weighing the available lines of evidence, the assessment determined that the current data are indicative of a causal effect.").

[28] *Id.* at 32-33; *see also id.* at 36 ("The human database provides differing results between case-control and cohort studies.").

[29] (FDA Denial Letter at 4 ("Results of case-control[] studies do not demonstrate a consistent positive association across studies.").)

perineal applications of talc," "none demonstrated both a clear dose-response trend and statistical significance."[30] And it further noted that "[t]he available human studies on possible migration of talc to the ovaries and presence of talc particles in the ovaries are indicative but not definitive."[31]

In any event, plaintiffs ignore that in a prior draft, Health Canada expressly noted that it applied "[p]recaution . . . to avoid the potential underestimation of risk due to a lack of information, thus ***erring on the side of being protective of human health*** and the environment."[32] The limited analysis of the Bradford Hill factors that plaintiffs highlight was expressly conducted in light of this purpose.[33]

As courts have repeatedly recognized, "regulatory findings and standards alone are insufficient to reliably establish general causation, as regulatory bodies are focused on protecting public health and thus err on the side of caution in determining what is safe." *Vandestreek v. Lockheed Martin Corp.*, No. 21-1570,

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30 Health Canada Screening Assessment at 33.

31 *Id.* at 44.

32 Health Canada, *Application of Weight of Evidence and Precaution in Risk Assessment*, https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/application-weight-of-evidence-precaution-risk-assessments.html (last modified Feb. 11, 2022) (emphasis added).

33 Health Canada Screening Assessment at 2 ("This screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific information and ***incorporating a weight of evidence approach and precaution***.") (emphasis added).

2023 WL 6396087, at *2 n.5 (M.D. Fla. Sept. 27, 2023), *appeal dismissed*, No. 23-13560, 2024 WL 1756018 (11th Cir. Feb. 7, 2024); *see also In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 387 F. Supp. 3d 323, 356 (S.D.N.Y. 2019) (explaining that regulatory agencies "often use[] a different standard than a court does to evaluate evidence of causation in a products liability action" and "may choose to err on the side of caution . . . upon a lesser showing of harm to the public than the preponderance-of-the-evidence . . . standard") (citation omitted); *In re Zantac (Ranitidine) Prods. Liab. Litig.*, 644 F. Supp. 3d 1075, 1285 (S.D. Fla. 2022) ("A regulatory agency such as the FDA may choose to err on the side of caution.") (citation omitted). Because a regulatory agency's prevention-oriented standards "involve[] a much lower standard than that which is demanded by a court of law," Health Canada's assessment is thus inapposite for establishing causation in litigation (or science). *In re Zantac*, 644 F. Supp. 3d at 1285; *see also Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002) (explaining that regulatory agencies employ a risk-utility analysis that is distinct from the scientific standard demanded by a court, which is "required by the *Daubert* trilogy to engage in objective review of evidence to determine whether it has sufficient scientific basis to be considered reliable").

This is especially true since the overwhelming majority of regulatory agencies (including the one in the United States with oversight over cosmetic

products) have rejected a determination of causality. For example, the FDA "did not find that the data submitted presented conclusive evidence of a causal association between talc use in the perineal area and ovarian cancer."[34] And the CDC's website does not list talc use as a risk factor for ovarian cancer.[35]

Lastly, plaintiffs posit that defense experts' testimony that the "methodologies for all experts today are the same as what was considered in 2019" "supports leaving Judge Wolfson's findings undisturbed." (Pls.' Br. at 10, 12.) But no one is disputing that the relevant methodology (Bradford Hill) is the same as what was considered previously. Rather, the question is whether plaintiffs carried their burden—by a preponderance of the evidence—of establishing that their "experts 'reliably ***applied***' Bradford Hill." *In re Onglyza*, 93 F.4th at 347 (emphasis added). And "[s]ince this litigation began, the science has developed in a way that further calls into question the causal hypotheses asserted by plaintiffs' experts."[36]

For all of these reasons, plaintiffs fail to demonstrate that Judge Wolfson's prior general causation *Daubert* ruling properly adhered to Rule 702.

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34 FDA Denial Letter at 1.

35 https://www.cdc.gov/ovarian-cancer/risk-factors/index.html.

36 (Decl. of Gregory Diette at 4, May 28, 2024 (Ex. 8 to Davidson Decl.).)

II. NEW SCIENTIFIC DEVELOPMENTS HIGHLIGHT THE NEED TO RECONSIDER THE PRIOR *DAUBERT* RULING.

Plaintiffs argue that the "new science"—including "post-2020 cohort studies" (O'Brien 2020, Woolen 2022 and O'Brien 2024)[37] and statements by Health Canada, IARC, the NIH and the EPA—support Judge Wolfson's prior ruling, going so far as to claim that the case for causation is "stronger" than what plaintiffs' experts claimed during the original *Daubert* proceeding. (Pls.' Br. at 12-17.) While plaintiffs contend that scientific developments bolster their experts' application of the Bradford Hill factors, the opposite is true.

A. New Evidence Confirms That The Association Is Weak, Not Strong.

Plaintiffs argue that O'Brien 2020, Woolen 2022 and O'Brien 2024 all "show a statistically significant increased risk of epithelial ovarian cancer with genital talc use," which supposedly reinforces their experts' claims that the association is sufficiently strong. (Pls.' Br. at 18.) However, these studies not only confirm that any relative risk posed by cosmetic talc is facially weak (i.e., not

[37] Plaintiffs' characterization of Woolen 2022 and O'Brien 2024 as "cohort studies" is facially wrong. Woolen 2022 is described by co-author and expert Dr. Smith-Bindman as a "systematic and quantitative meta-analytic review" (3d Am. Rep. of Rebecca Smith-Bindman at 23, May 28, 2024 (Ex. 9 to Davidson Decl.)), and O'Brien 2024 included "a mix of retrospective and prospective information," O'Brien 2024 at 13.

strong), but also demonstrate why any such association is even weaker than what is being reported.

O'Brien 2020. Plaintiffs argue that O'Brien 2020 "shows a positive association between genital talc use and ovarian cancer, with a statistically significant risk in women with intact reproductive system." (Pls.' Br. at 19.) But O'Brien found "no statistically significant association between . . . use of [talcum] powder in the genital area and risk of ovarian cancer."[38] The estimated HR for long-term use vs never use was 1.01 (95% CI, 0.82-1.25), with a non-statistically significant estimated HR of 1.09 (95% CI, 0.97-1.23) for frequent vs never users.[39] In other words, O'Brien found that there was a non-statistically significant increased risk of 9%, which is a "far smaller" risk than ones "identified by [other] experts" in other cases where opinions on strength were deemed unreliable. *See, e.g.*, *In re Acetaminophen I*, 2023 U.S. Dist. LEXIS 224899, at *81-82 (distinguishing "risk ratios between 1.0 and 2.0" from ones where the risk ratio was 7.69, 3.90 and 2.2).

Plaintiffs nevertheless claim that the authors "clarified that their overall findings were positive and likely underestimated the true risk of association." (Pls.' Br. at 22.) But the authors of O'Brien 2020 published an article in the

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38 O'Brien 2020 at 56.

39 *Id.* at 49.

journal *Gynecologic Oncology* just a few years later in which they stated: "[g]iven the inability to attribute a clear causal factor to the observed associations, the lack of a good experimental model, the lack of a specific biomarker for powder-related carcinogenesis, and the inability to rule out confounding by indication, ***it is difficult to conclude that the observed associations are causal***. Furthermore, given the widespread use of powders and the rarity of ovarian cancer, the case for public health relevance is limited."[40]

While plaintiffs point to statements made by the O'Brien 2020 authors in response to one of plaintiffs' general causation experts, Dr. Harlow, these statements do not remotely purport to endorse the opinions being offered in this litigation. For example, plaintiffs highlight the fact that the authors "never equated the lack of statistical significance to evidence of no association." (Pls.' Br. at 22 (citation omitted); *id.* at 23.) But the question is whether the association is sufficiently strong to support plaintiffs' burden of proving causation—and as O'Brien 2020 makes clear, the answer is no. Indeed, plaintiffs even quote multiple statements from NIH authors describing the association reported in O'Brien 2020 as "small" and "***very small***." (*Id.* at 23 (quoting Pls.' Br. Ex. 16 and O'Brien 2024).)

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[40] Wentzensen & O'Brien 2021 at 207 (emphasis added).

Woolen 2022. Plaintiffs also tout Woolen 2022—a study co-authored by one of plaintiffs' general causation experts, Dr. Smith-Bindman—which found that "frequent use of perineal talcum powder was associated with an increased risk of ovarian cancer, with a pooled adjusted odds ratio of 1.47 (CI 1.31-16.65)." (Pls.' Br. at 27 (quoting Woolen 2022 at 2530).) But even this reported relative risk is a far cry from the examples of a nine-, ten-, or even 200-fold increase in risk that Hill originally identified as supportive of causation, and is "undeniably . . . not a strong association." *In re Viagra (Sildenafil Citrate) & Cialis (Tadalafil) Prods. Liab. Litig.*, 424 F. Supp. 3d 781, 796 (N.D. Cal. 2020) ("the risk factor that emerged across all the studies was somewhere around 1.2," which "undeniably is not a strong association"). Moreover, the NCI—which considered Woolen 2022 and concluded that the "data are inadequate to support an association" between talc use and increased ovarian cancer risk—found that "because of the structure of [Woolen 2022's] analysis, ***the results should be interpreted with care***."[41] As the NCI PDQ points out, the authors only included a "highly selected subset analysis of" O'Brien 2020 that "was inconsistent with the main findings of" O'Brien 2020 (the subgroup of patent women).[42] There are other methodological concerns with

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41 NCI 2024 PDQ (emphasis added).

42 *Id*. (*See also* Dep. of Rebecca Smith-Bindman ("3/20/24 Smith-Bindman Dep.") 70:1-9, Mar. 20, 2024 (Ex. 10 to Davidson Decl.).)

Woolen 2022 as well. Most notably, the authors arbitrarily defined "frequent" talc use after Dr. Smith-Bindman had reviewed the literature to prepare her litigation report—and did so in a way that excluded most of the cohort study data.[43] Moreover, despite this stated definition, Dr. Smith-Bindman admitted that where a study provided multiple sets of data that fit their arbitrary definition of "frequent use," the Woolen 2022 authors only included data from the "highest use" category.[44] Scientists are very skeptical of "post hoc analyses" like Woolen 2022, because the authors can manipulate their selection criteria based on their desired result.

O'Brien 2024. Plaintiffs also highlight O'Brien 2024, which found a "positive association between genital talc use and ovarian cancer." (Pls.' Br. at 24 (quoting O'Brien 2024 at 13).) The authors of that study sought to rely on retrospective surveys to obtain more information on talc use from women in the Sister Study, but many respondents either provided contradictory responses or failed to respond to the follow-up survey. In an effort to address the significant amount of missing data, the paper modeled various scenarios using data that were largely "imputed"—i.e., made up. In short, O'Brien 2024 is, at bottom,

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[43] Woolen, *Association Between the Frequent Use of Perineal Talcum Powder Products and Ovarian Cancer: a Systematic Review and Meta-analysis*, 37(10) J. Gen. Intern. Med. 2526, 2526 (2022) ("Woolen 2022") (Pls.' Br. Ex. 12).

[44] *Id.* at 2527. (3/20/24 Smith-Bindman Dep. 61:22-62:25.)

guesswork; presumably for that reason, the authors cautioned that the "***results do not establish causality and do not implicate any specific cancer-inducing agent***."[45]

Additional Studies Ignored By Plaintiffs. There are additional studies published after Judge Wolfson's *Daubert* ruling—none of which plaintiffs address in their brief—which provide additional evidence that recall bias is to blame for any reported weak association in the case-control studies that plaintiffs' experts rely on to form their causation opinions. For example:

- O'Brien 2023 "collected retrospective data on douching and genital talc use" and evaluated the reliability and consistency of self-reported exposure data used in observational studies. The authors reported that recall bias is "potentially driving some of the previously observed differences in effect estimates between studies collecting genital powder exposure status retrospectively versus prospectively."[46]

- Goodman 2024 adjusted the reported findings in Cramer 2016 (a case-control study touted by plaintiffs' experts) for several plausible recall bias models and reported that the results were no longer statistically significant (except in one model, which reported a significant ***protective*** effect), which "demonstrates that recall bias alone may have a large impact on risk estimates" in case-control studies and "that recall bias results in a bias away from the null" (i.e., away from a finding of no association).[47]

- Davis 2021—a study co-authored by plaintiffs' expert, Dr. Moorman—described that "[w]hen the time period was limited to

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45 O'Brien 2024 at 13 (emphasis added); *see also id.* at 14 ("[O]ur findings . . . do not pinpoint a specific cause or mechanism . . . .").

46 O'Brien 2023 at 376, 378, 383.

47 Goodman 2024 at 2-3.

> women who were interviewed prior to 2014 (i.e., before ongoing lawsuits about genital powder use which had extensive media coverage), the results were attenuated and no[t] . . . significant."[48] For this reason, the Davis authors only included data from individuals interviewed prior to 2014 "to avoid possible reporting bias resulting from lawsuits."[49]

Recent studies (e.g., Chang 2024) also demonstrate that confounding may explain any positive associations reported in case-control studies. In Chang, the authors noted that within the hygiene product category, the ***only*** product significantly associated with ovarian cancer was douche,[50] suggesting that if there is an increased risk of ovarian cancer from personal care products, ***the association is with douching***, which most studies did not account for.

In short, new evidence published after Judge Wolfson's general causation *Daubert* ruling provides additional evidence that any relative risk posed by cosmetic talc is facially weak (i.e., not strong) and over-inflated, such that Judge Wolfson's opinion on the issue should be revisited.

B. New Evidence Confirms That The Data Are Inconsistent.

Scientific developments since the prior *Daubert* ruling highlight the diametrically opposed nature of the studies assessing genital talc use and ovarian cancer. For example, the NCI's most recent PDQ reaffirms that the "[r]esults from

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48 Davis 2021 at 1664-65.

49 *Id.* at 1665-66.

50 *See* Chang 2024 at 5.

case-control and cohort studies are ***inconsistent***."[51] Micha 2022 likewise observed that "clinical research has accorded ***inconsistent findings***," which makes a conclusion that the observed association is causal "untenable."[52] And as Goodman 2024 recently recognized, "[c]ohort studies have consistently reported no overall association and no exposure-response relationship between perineal talc use and ovarian cancer risk overall."[53]

Plaintiffs nevertheless argue that O'Brien 2024 and IARC's recent statements validate Judge Wolfson's prior finding that there is reliable evidence of "consistency" between the studies of genital talc use and ovarian cancer. (Pls.' Br. at 27-30.) But both only further confirm the disparate nature of the epidemiologic data.

O'Brien 2024. According to plaintiffs, "the NIH Sisters Study investigators" observed in O'Brien 2024 a reported association that is "consistent with" what has been reported in previous meta-analyses and pooled analyses of

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51 NCI 2024 PDQ.

52 Micha, *Talc Powder and Ovarian Cancer: What is the Evidence?*, 306 Arch. Gynecol. Obstet. 931, 932 (2022) ("Micha 2022") (Ex. 11 to Davidson Decl.).

53 Goodman 2024 at 3; *see also* Lynch, *Systematic Review of the Association Between Talc and Female Reproductive Tract Cancers*, 5 Frontiers in Toxicology 1, 7 (2023) (Ex. 12 to Davidson Decl.) ("None of the five prospective cohort studies reported any statistically significant associations between genital talcum powder use and risk of epithelial ovarian cancer, and relative risk estimates were close to unity.").

case-control studies. (Pls.' Br. at 29 (quoting O'Brien 2024 at 13).) But the ***actual*** data generated by the Sister Study cohort show an "inverse or weakly positive association[] between [talc] and all cancers of interest."[54] Indeed, the only non-imputed prospective data in the study reported no association. Thus, at most, O'Brien 2024 highlights inconsistencies in the body of literature, and plaintiffs' experts' willingness to reach conclusions that the O'Brien authors "d[id] not make" "betray[s] a 'lack of scientific rigor.'" *In re Onglyza*, 93 F.4th at 346 (citation omitted).

IARC. Plaintiffs tout a recent article about the IARC working group's findings, which referenced "consistent positive associations for ever-use versus never-use . . . in pooled cohort studies and case control studies." (Pls.' Br. at 29 (quoting Stayner 2024 at 2).) Plaintiffs fail to note, however, IARC's statement that "a causal role for talc could ***not*** be fully established" in light of "biases in how talc use was reported in the epidemiological studies."[55] As explained above, recent scientific literature has repeatedly acknowledged "that recall bias alone may have a

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[54] O'Brien 2024 at 12; *see also* Gonzalez, *Douching, Talc Use, and Risk of Ovarian Cancer*, 27(6) Epidemiology 797, 800-02 (2016) ("Gonzalez 2016") (Ex. 13 to Davidson Decl.) (HR 0.73 (95% CI: 0.44-1.2)).

[55] IARC Press Release (emphasis added). Because the IARC monograph with the new classification will not be published until some unspecified date in 2025, it is impossible to fully evaluate the decision-making process behind this change.

large impact on risk estimates" in case-control studies[56] and is contriving any alleged consistency amongst those studies—i.e., recall bias is "driving some of the previously observed differences in effect estimates between studies collecting genital powder exposure status retrospectively versus prospectively."[57] Katie O'Brien (a member of the IARC working group and co-author of the two O'Brien studies just discussed) echoed the IARC press release, stating that "the human study evidence was ***not*** strong enough to say that talc causes ovarian cancer."[58]

In an effort to recharacterize the new scientific evidence, plaintiffs once again distort defendants' position regarding statistical significance and posit that "positive" associations—regardless of statistical significance—suffice for consistency purposes. (Pls.' Br. at 28.) But it is not only statistical significance that renders the results inconsistent, because point estimates (which have nothing to do with significance) are consistently lower in cohort studies than case-control studies, a fact underscored by new scientific developments.[59] And just as

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56 Goodman 2024 at 2-3.

57 O'Brien 2023 at 378, 383.

58 O'Brien Statement (emphasis added); *see also* Stayner 2024 at 2 (summarizing IARC's reclassification, which was based on "'***limited***' evidence that talc causes ovarian cancer in humans" and cautioning that "bias from differential exposure misclassification could not be excluded based on a bias analysis conducted by the Working Group and confounding by asbestos contamination of the talc also could not be ruled out") (emphasis added).

59 *See, e.g.*, O'Brien 2020.

importantly, caselaw since Judge Wolfson issued her original ruling confirms that "it is not for the courts to be the pioneers, forging new trails in scientific thinking, especially when that means departing from well-established research principles, such as the principle of statistical significance." *In re Acetaminophen I*, 2023 U.S. Dist. LEXIS 224899, at *122 (citation omitted); *see also In re Zantac*, 644 F. Supp. 3d at 1222 (excluding Drs. McTiernan and Moorman for "routinely . . . disregard[ing] the concept of statistical significance"); *In re Paraquat*, 2024 WL 1659687, at *38 (excluding an expert who "fail[ed] to engage" with the "lack of statistical significance . . . throughout the epidemiological literature") (citing *In re Acetaminophen I*); *In re Acetaminophen - ASD-ADHD Prods. Liab. Litig.*, MDL No. 3043, 2024 U.S. Dist. LEXIS 121259, at *68 (S.D.N.Y. July 10, 2024) ("*In re Acetaminophen II*") ("[I]gnor[ing] statistical significance . . . is not a reliable application of scientific methodology.").

In short, recent scientific developments further highlight the inconsistency and overall unreliability of the evidence on general causation.

C. Recent Evidence Undermines The Plausibility Of Plaintiffs' Experts' Mechanism Theory.

Plaintiffs also still cannot point to any reliable support for their theories that: (1) talc can move through the body against gravity and end up in the ovaries; (2) talc causes chronic inflammation or oxidative stress in vitro or in animals, much less in humans; and (3) any observed changes in inflammation or oxidative stress

markers lead to mutations or neoplastic transformation, much less to full-blown carcinogenesis. Indeed, as Health Canada acknowledged, "[t]he available human studies on possible migration of talc to the ovaries and presence of talc particles in the ovaries are . . . not definitive."[60]

Plaintiffs nonetheless claim that "[a] couple of examples in the post-2020 peer-reviewed literature" "strengthen Judge Wolfson's conclusion for 'biologic plausibility.'" (Pls.' Br. at 30.) Not so. At most, these examples show that "[s]cientists ha[d] at best developed hypotheses," none of which has advanced to the stage of scientific proof. *In re Acetaminophen I*, 2023 U.S. Dist. LEXIS 224899, at *90-91 (excluding opinions on biological plausibility). Moreover, none of the papers cited by plaintiffs offers new research on biological plausibility; instead, they are epidemiological or review articles with mere passing references to old mechanistic hypotheses. Because such statements in the literature are "no more reliable" than the underlying data they report, *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 542 (W.D. Pa. 2003), these articles do not move the needle.

For example, plaintiffs cite O'Brien 2020, an epidemiology paper that contains a single line about inflammation based on a reference to a 25-year-old review article. (Pls.' Br. at 30-31.) But the O'Brien 2020 authors explicitly

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60 Health Canada Screening Assessment at 44.

recognized that it was a mere "hypothesis" that "powder with or without asbestos could irritate and inflame the reproductive tract," and cautioned that their findings regarding the means by which talc could travel to the ovaries "should be considered only exploratory and hypothesis generating."[61] Plaintiffs also cite to O'Brien 2021, in which the authors "hypothesized that genital talc use could incite an inflammatory response and promote carcinogenesis"[62] and quote a review article by Sánchez-Prieto for the speculative proposition that talc "***might*** ascend through the genital tract" where it "***could possibly*** trigger an inflammatory response." (Pls.' Br. at 31 (emphasis added).)[63] And they rely on Phung 2022 for the throwaway line that "inflammation ***has been proposed*** as a possible biologic mechanism."[64] (Pls.' Br. at 31-32 n.67.) The fact that something has been "proposed" does not make it plausible, and the only article Phung 2022 cites for this proposition actually concluded that "chronic inflammation ***does not*** play a

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61 O'Brien 2020 at 56-57.

62 O'Brien, *The Association Between Douching, Genital Talc Use, and the Risk of Prevalent and Incident Cervical Cancer*, 11(1) Sci. Rep. 1, 7 (2021) (Pls.' Br. Ex. 15).

63 Citing Sánchez-Prieto, *Etiopathogenesis of Ovarian Cancer. An Inflamm-aging Entity?*, 42 Gynecol. Oncol. Rep. 101018 (2022) (Pls.' Br. Ex. 19). Notably, Sánchez-Prieto, which, as noted, is a review article, not a report of original research, contains no citation for this proposition.

64 Phung, *Effects of Risk Factors for Ovarian Cancer in Women With and Without Endometriosis*, 118(5) Fertil. Steril. 960, 965 (2022) (Pls.' Br. Ex. 20).

major role in the development of ovarian cancer."[65] Lastly, although Ogunsina 2023 states that talc can cause inflammation in "animal models" "once deposited onto epithelial cells" (Pls.' Br. at 31), [66] that statement is only supported by a citation to the 2010 IARC monograph,[67] which is not new and also does not support a claim of inflammation in humans.

For these reasons, the new scientific evidence offers no reliable support for plaintiffs' proffered causal theories.

D. Recent Evidence Further Highlights The Lack Of A Dose-Response Relationship.

Recent scientific evidence further undermines plaintiffs' experts' claims that there is a dose-response relationship between cosmetic talc exposure and the development of ovarian cancer. For example:

- O'Brien 2020 found "no clear dose-response trends for duration and frequency of powder use in the genital area in relation to ovarian cancer risk."[68]

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65 Merritt, *Talcum Powder, Chronic Pelvic Inflammation and NSAIDs in Relation to Risk of Epithelial Ovarian Cancer*, 122(1) Int'l J. Cancer 170, 175 (2008) (Ex. 14 to Davidson Decl.).

66 Ogunsina, *Association of Genital Talc and Douche Use in Early Adolescence or Adulthood with Uterine Fibroids Diagnoses*, 229(6) Am. J. Obstet. Gynecol. 665.e1, 665.e1 (2023) (Pls.' Br. Ex. 9).

67 The citation is to pages "1-413" of the monograph, so it is impossible to know what exactly the authors intend to refer to. *See id.* at 665.e1 & Reference 19.

68 O'Brien 2020 at 56.

- Davis 2021 (co-authored by Dr. Moorman) reported that "[t]here was not a dose-response relationship regarding frequency or duration of genital powder use and ovarian cancer."[69]

- Woolen 2022 (co-authored by Dr. Smith-Bindman) reported just two years ago that the "[r]isk of ovarian cancer in women with frequent perineal talcum powder product"—i.e., dose-response—"is not well understood."[70]

- Health Canada—which plaintiffs tout heavily in their brief—concluded that among "studies that provided some evidence of increased risk of ovarian cancer with increasing perineal applications of talc," "none demonstrated both a clear dose-response trend and statistical significance."[71]

- NCI observed that in multiple meta- and pooled-analyses, a case-control study and cohort studies examining the association between talcum powder use and ovarian cancer, "a dose-response relationship was not found" and "there was no evidence of increasing risk with increasing frequency of use."[72]

Plaintiffs nonetheless argue that "both O'Brien (2024) and Woolen (2022) showed a dose response." (Pls.' Br. at 33.) They did not. Only after the O'Brien 2024 authors imputed a number of "corrections" and assumptions into the Sister Study cohort data (i.e., after they made up data to plug in research holes) did the authors observe "dose-response patterns."[73] The ***actual*** data generated by the

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69 Davis 2021 at 1661, 1663-65.

70 Woolen 2022 at 2526 (emphasis added).

71 Health Canada Screening Assessment at 33.

72 NCI 2024 PDQ.

73 O'Brien 2024 at 13.

Sister Study cohort did not demonstrate a dose-response relationship, and in fact showed an "inverse or weakly positive associations between [talc] and all cancers of interest."[74] And although Woolen 2022 purported to "estimate the association between frequent" talc use and ovarian cancer,[75] it "didn't evaluate the dose response," as Dr. Smith-Bindman (a co-author) conceded.[76] As such, plaintiffs are improperly drawing "conclusions that study authors were not willing to make." *In re Acetaminophen I*, 2023 U.S. Dist. LEXIS 224899, at *105; *see also In re Onglyza*, 93 F.4th at 346 (excluding expert, who "drew 'unauthorized . . . conclusions the authors of the study d[id] not make,' betraying a 'lack of scientific rigor'") (citation omitted).

In short, ample recent scientific developments further highlight the lack of any dose-response relationship between talcum powder use and ovarian cancer and the overall unreliability of plaintiffs' experts' general causation opinions.

E. "Authoritative" Scientific Bodies Do Not Support A Causal Effect.

Plaintiffs lastly assert that "actions" by scientific bodies—including Health Canada, IARC, the NIH and the EPA—"further support[] a causal effect." (Pls.'

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74 *Id.* at 12; *see also* Gonzalez 2016 at 800-02 (HR 0.73 (95% CI: 0.44-1.2)).

75 Woolen 2022 at 2526.

76 (3/20/24 Smith-Bindman Dep. 153:3-5; *see also* Dep. of Rebecca Smith-Bindman 227:13-16, Oct. 1, 2021 (Ex. 15 to Davidson Decl.).)

Br. at 34.) But none of these bodies has determined that talc use causes ovarian cancer. To the contrary, IARC made it clear that "a causal role for talc could ***not*** be fully established" in light of "biases in how talc use was reported in the epidemiological studies."[77] Similarly, O'Brien 2024 explicitly cautioned that its imputed "results do not establish causality and do not implicate any specific cancer-inducing agent."[78] And Health Canada merely states that "[t]he available data are indicative of a causal effect."[79] Health Canada also expressly noted evidence that undermines any finding of causation, including that: "there is some inconsistency between results from case-control studies versus cohort studies, in particular with respect to the degree of statistical significance";[80] among "studies that provided some evidence of increased risk of ovarian cancer with increasing perineal applications of talc," "none demonstrated both a clear dose-response trend

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77 IARC Press Release (emphasis added). Because the IARC monograph with the new classification will not be published until some unspecified date in 2025, it is impossible to fully evaluate the decision-making process behind this change.

78 O'Brien 2024 at 13; *see also id.* at 14 ("[O]ur findings . . . do not pinpoint a specific cause or mechanism . . . .").

79 Health Canada Screening Assessment at 36; *id.* at 45 ("While there may not be consensus within the scientific community regarding the interpretation of the epidemiological information, after weighing the available lines of evidence, the assessment determined that the current data are indicative of a causal effect.").

80 *Id.* at 32; *see also id.* at 36 ("The human database provides differing results between case-control and cohort studies.").

and statistical significance";[81] and "[t]he available human studies on possible migration of talc to the ovaries and presence of talc particles in the ovaries are . . . not definitive."[82] Lastly, the EPA never evaluated whether cosmetic use of talc can cause ovarian cancer; nor did it conclude that asbestos is present in any cosmetic talc products.

Consistent with these findings, other regulatory bodies—including the FDA and CDC—have rejected casualty.[83] And numerous medical bodies—including the American College of Obstetricians and Gynecologists, the Society of Gynecologic Oncology, the National Comprehensive Cancer Network, the National Cancer Institute and the American Cancer Society—have recently reiterated their rejection of plaintiffs' proffered causal theory.[84]

In any event, even if actions by Health Canada, IARC, the NIH and the EPA could be interpreted as supporting plaintiffs' theories of causation—and they cannot—their interpretations of the available evidence are inapposite for establishing causation in litigation (or science) because a regulatory agency's

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81 Health Canada Screening Assessment at 33.

82 *Id.* at 44.

83 FDA Denial Letter at 4; https://www.cdc.gov/ovarian-cancer/risk-factors/index.html.

84 https://www.acog.org/womens-health/faqs/ovarian-cancer; https://www.sgo.org/patients-caregivers-survivors/caregivers/ovarian-cancer-risk-factors/; NCCN Guidelines; NCI 2024 PDQ; Cancer Facts & Figures 2024, at 23.

prevention-oriented standards "involve[] a much lower standard than that which is demanded by a court of law," as discussed in Section I above. *In re Zantac*, 644 F. Supp. 3d at 1285; *Vandestreek*, 2023 WL 6396087, at *2 n.5 ("[R]egulatory findings and standards alone are insufficient to reliably establish general causation, as regulatory bodies are focused on protecting public health and thus err on the side of caution in determining what is safe."). For this reason, too, plaintiffs' effort to invoke regulatory agencies to salvage their experts' theories should be rejected.

CONCLUSION

For the foregoing reasons, plaintiffs' motion should be denied.

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Respectfully submitted,

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